

Electronic supplementary material

Title: Desloratadine exposure and incidence of seizure – A Nordic post-authorization safety study using a new-user cohort study design, 2001-2015

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Supplementary Table S1 Overview of year of establishment of the national registries used in the present study, data extraction period and the study period.

| National registry | Year of establishment of the registries by country | | | |
|--------------------------------|--|---------------------------|------------------------|---------------------------|
| | Denmark | Finland | Norway | Sweden |
| Civil Registration System | 1968 | 1967 | 1964 | 1965 |
| National Prescription Registry | 1995 | 1994 | 2004 | 2006 |
| National Patient Registry | 1977 (1995 ^a) | 1967 (1998 ^b) | 2008 | 1987 (2001 ^c) |
| ICD-8 codes | 1977–1993 | 1967–1986 | - | - |
| ICD-9 codes | - | 1987–1995 | - | 1987–1996 |
| ICD-10 codes | 1994–present | 1996–present | 2008–present | 1997–present |
| Data extraction period | 1977–2015 | 1967–2015 | 2008–2015 | 1987–2015 |
| Study period | 2001–2015 | 2001–2015 | 2010–2015 ^d | 2006–2015 |
| (number of years included) | (15 years) | (15 years) | (6 years) | (11 years) |

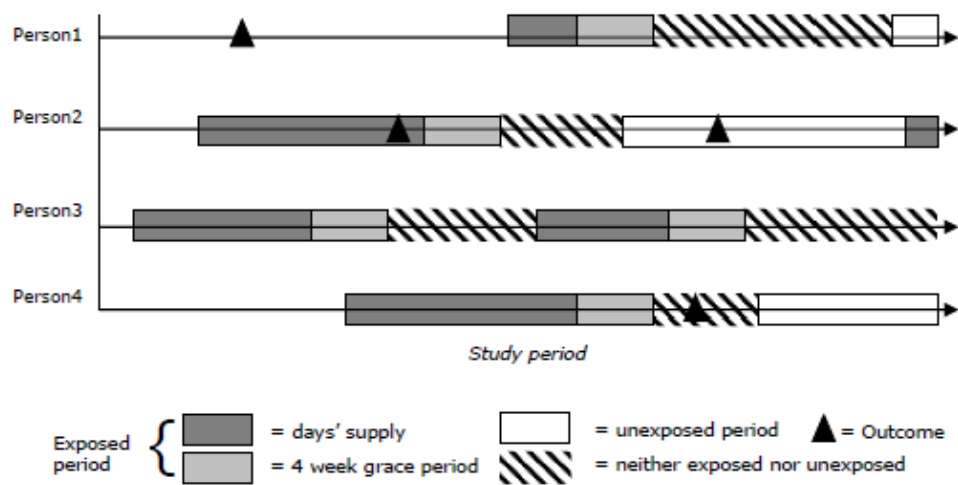
^aContacts with outpatient clinics (incl. emergency departments) since 1995

^bContacts with outpatient clinics (incl. emergency departments) since 1998

^cContacts with outpatient clinics (incl. emergency departments) since 2001

^dStudy period in Norway starts in 2010 due to applying a minimum of a 2-year disease-free look-back period to obtain incident outcomes.

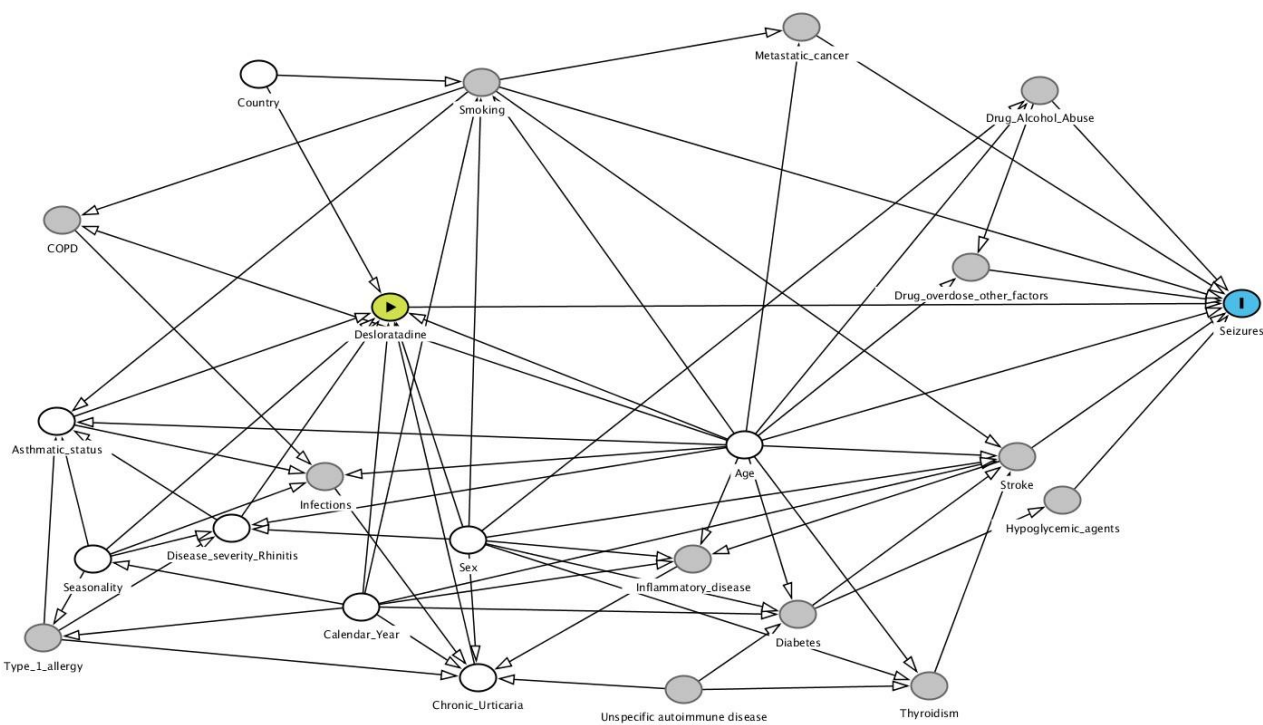
Supplementary Figure S1 Illustration of study design.



Supplementary Figure S2 Directed acyclic graph (DAG) of confounders included in the analysis of the association between desloratadine exposure and seizures.

Confounders included were based on the minimum sufficient adjustment set identified.

Desloratadine exposure is mapped with a triangle within the yellow circle, seizures as outcome is mapped with a vertical line within the blue circle and the selected set of potential confounders is mapped in bold white circles. Potential confounders not included in the analysis are mapped in grey circles.



Supplementary Table S2 Definition of variables (exposure, outcome, potential confounders and exclusion criteria) by Anatomical Therapeutic Classification (ATC) and International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes for desloratadine exposure, seizure as outcome and confounders in the study.

| Variable | Registry | Classification system ^a | Codes ^b |
|------------------------|--------------|------------------------------------|--------------------------|
| Exposure | | | |
| Desloratadine | Prescription | ATC | R06AX27 |
| Outcome variables | | | |
| Seizures | Patient | ICD-10 | R56* |
| Febrile seizure | | | R560* |
| Non-febrile seizure | | | R568* |
| Potential confounders | | | |
| Asthma | Prescription | ATC | R03A*, R03B* |
| | Patient | ICD-8 | 4930* |
| | | ICD-9 | 493* |
| | | ICD-10 | J45* |
| Severe rhinitis | Prescription | ATC | V01AA* (excl V01AA07) |
| Chronic urticaria | Patient | ICD-8 | 70890*, 70891* |
| | | ICD-9 | 708*, 709* (excl 6927) |
| | | ICD-10 | L50*, L563* (excl L508D) |
| Exclusion criteria | | | |
| Epilepsy | Patient | ICD-8 | 34509*–34511* |
| | | ICD-9 | 345* |
| | | ICD-10 | G40* |
| Antiepileptic medicine | Prescription | ATC | N03A*, N05BA* |
| Malignant brain tumor | Patient | ICD-8 | 1910* |
| | | ICD-9 | 1990*–1919* |
| | | ICD-10 | C70*, C71* |

| Variable | Registry | Classification system ^a | Codes ^b |
|---|--------------|------------------------------------|--|
| Benign brain tumor | Cancer | ICD-7 | 193*, 1921*–1923*, 1910*–1919* |
| | | ICD-10 | C70*, C71* |
| | Patient | ICD-8 | 2250* |
| | | ICD-9 | 2250* |
| | | ICD-10 | D330*–D332* |
| Head trauma | Patient | ICD-8 | 85119* |
| | | ICD-9 | 800*–804*, 850*–854* |
| | | ICD-10 | S06* |
| Other antihistamines than desloratadine | Prescription | ATC | R06AE07, R06AE09, R06AX12, R06AX13, R06AX18, R06AX22, R06AX25, R06AX26, R06AX28, R06AX29 |

^aICD-8 codes were used in 1969–1993 in Denmark, 1969–1986 in Finland and Sweden. ICD-9 codes were used in 1987–1995 in Finland and in 1987–1996 in Sweden and never used in Denmark. ICD-10 codes were used in 1994–present in Denmark, in 1996–present in Finland and 1997–present in Sweden. All sub-codes for the listed codes were included. ATC= Anatomic Therapeutic Chemical, ICD=International classification of diseases

^bAll subcodes included